

Claims

1. A method of diagnosis comprising:

(a) providing a biological sample from a human identified as being in need of treatment with a therapeutic agent that is transported by OATP-C, wherein the sample comprises a nucleic acid encoding OATP-C;

(b) testing the nucleic acid for the presence, on at least one allele, of either

(i) a codon encoding alanine at the position corresponding to position 174 of SEQ ID NO:1, or

10 (ii) an allele of a polymorphism in linkage disequilibrium with (i); and

(c) if either (i) or (ii) is found in at least one allele, diagnosing the human as likely to have reduced ability to transport the therapeutic agent into cells.

2. A method according to claim 1 wherein the polymorphism of (b)(ii) is -26A>G, -118A>C, -309T>C, -878A>G, -903C>T, -1054G>T, -1215T>A, or -1558T>C, all of SEQ ID NO:2; or T2122G, C2158T, A2525C, or G2651A, all of SEQ ID NO:3.

3. A method according to any preceding claim wherein the polymorphism of (b)(ii) is selected from -118A>C and -1558T>C of SEQ ID NO:2.

20 4. A method according to any preceding claim wherein the therapeutic agent is a statin, the human is being treated with one dose level of statin and step (c) further comprises diagnosing the human as suitable for titration to another higher statin dose level comprising monitoring for a decrease in benefit-risk ratio resulting from the reduced ability to transport 25 the statin into cells.

5. A method according to any preceding claim wherein the therapeutic agent is rosuvastatin.

30 6. A method according to any preceding claim wherein the therapeutic agent is atorvastatin, cerivastatin, fluvastatin, pravastatin, or simvastatin.

7. A method according to claim 5 wherein the human is being treated with at least 5 mg of a rosuvastatin daily.
8. A method according to claim 5 wherein the human is being treated with at least 10 mg of a rosuvastatin daily.
9. A method according to claim 5 wherein the human is being treated with at least 20 mg of a rosuvastatin daily.
- 10 10. A method according to claim 5 wherein the human is being treated with at least 40 mg of a rosuvastatin daily.
11. A method of diagnosis comprising:
 - (a) providing a biological sample from a human identified as being in need of treatment with a therapeutic agent that is transported into cells by OATP-C, wherein the sample comprises an OATP-C polypeptide;
 - (b) determining whether the amino acid of OATP-C corresponding to position 174 of SEQ ID NO:1 is a valine; and
 - (c) if the amino acid is not a valine, diagnosing the human as likely to have a reduced ability to transport the therapeutic agent into cells.
12. A method according to claim 11 wherein the therapeutic agent is a statin, the human is being treated with one dose level of statin and step (c) further comprises diagnosing the human as suitable for titration to another higher statin dose level comprising monitoring for a decrease in benefit-risk ratio resulting from the reduced ability to transport the statin into cells.
13. A method according to claim 12 further comprising measurement of the level of OATP-C polypeptide with valine and/or alanine at position 174 whereby to determine the presence or absence of -118A>C polymorphism in OATP-C nucleic acid.

14. A method according to claim 12 further comprising measuring OATP-C polypeptide for presence or absence of OATP-C *15 allele whereby to determine the presence or absence of -118A>C polymorphism in OATP-C nucleic acid.

5 15. A method according to any one of claims 12-14 wherein the amino acid at position 174 is determined to be alanine.

16. A method according to any preceding claim wherein the therapeutic agent is rosuvastatin.

10

17. A method according to any preceding claim wherein the therapeutic agent is atorvastatin, cerivastatin, fluvastatin, pravastatin, or simvastatin.

18. A method according to claim 16 wherein the human is being treated with at least 5 mg 15 of a rosuvastatin daily.

19. A method according to claim 16 wherein the human is being treated with at least 10 mg of a rosuvastatin daily.

20 20. A method according to claim 16 wherein the human is being treated with at least 20 mg of a rosuvastatin daily.

21. A method according to claim 16 wherein the human is being treated with at least 40 mg of a rosuvastatin daily.

25